Journal of Pediatric Surgery Case Reports 31 (2018) 49–51

Contents lists available at ScienceDirect

Journal of Pediatric Surgery Case Reports

journal homepage: www.elsevier.com/locate/epsc

Papillary cystadenoma of the epididymis in a 12-year-old survivor of stage IV neuroblastoma

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ARTICLE INFO

Keywords:
Papillary cystadenoma
Epididymis
Prepubertal male
Neuroblastoma

ABSTRACT

Papillary cystadenoma of the epididymis (PCE) is the second most common benign neoplasm of the epididymis [1]. It is very uncommon and has never been reported in a prepubertal male. It may occur sporadically, but more often occurs in association with von Hippel- Lindau (VHL) disease [2]. There have been over 60 reports of patients with such tumors, with the youngest patient being 16 years old.

We present the case of a 12- year old male with a history of stage IV neuroblastoma. He presented with a left paratesticular mass that was discovered on routine follow up physical exam with his pediatric oncologist. He was asymptomatic at the time of presentation with no signs or symptoms of hypoandrogenism. A computed tomography scan of the abdomen and pelvis was negative for lymphadenopathy and additional disease sites. Given the patient's history of stage IV neuroblastoma, there was suspicion of yolk sac tumor or metastases; he underwent an open radical left orchiectomy. Frozen section was consistent with yolk sac tumor, however final pathology revealed normal testicle with PCE.

To date, this patient is the youngest reported patient with this diagnosis; furthermore papillary cystadenoma of the epididymis has never been reported in a patient with neuroblastoma.

1. Introduction

Testicular and paratesticular tumors are rare in prepubertal males, and represent 1–2% of the solid tumors in the pediatric population. Benign neoplasms (the most common of which are leiomyoma, fibroma, lipoma, hemangioma) should be distinguished from malignant tumors including leiomyosarcoma, fibrosarcoma, liposarcoma, rhabdomyosarcoma and metastatic disease as it may be possible to spare the testis during resection of the former. Only a minority of paratesticular tumors arise from the epididymis and the majority of these are benign mesenchymal neoplasms (i.e. adenomatoid tumor) [2]. Papillary cystadenoma(PCE), the second most common epididymal tumor, is an extremely rare, benign tumor of epithelial origin first described in 1956 in a 21-year-old male [1]. To date, fewer than 80 cases have been reported, two-thirds of these occurring in association with Von Hippel Lindau (VHL) syndrome.

PCE develops in the efferent ductules of the epididymis and typically presents as a painless, slowly growing, scrotal mass in a postpubertal male. Genetically it is associated with an allelic loss of the VHL gene [3]. Histologically, papillary cystadenoma resembles renal cell carcinoma and requires immunohistochemical distinction. Of the reported cases, about 40% were bilateral and 75% of these bilateral cases occurred in conjunction with VHL. Treatment of PCE consists of testicle sparing surgical excision with longitudinal surveillance due to a report of recurrence and two reports of transformation to cystadenocarcinoma [2]. To date, there have been no reports of cases of epididymal papillary cystadenoma in a prepubertal male.

2. Case report

A 12-year-old male with a history of stage IV high risk neuroblastoma, diagnosed eleven years prior to his current presentation and status post left adrenalectomy, right hepatectomy, chemotherapy, total body irradiation, and stem cell transplant, presented to his

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https://doi.org/10.1016/j.epsc.2017.12.010
Received 4 December 2017; Accepted 9 December 2017
Available online 12 December 2017

endocrinologist for routine survivorship follow-up. On physical exam, a nontender left paratesticular mass was palpated posterior to the testicle. There were no overlying skin changes to the scrotum and there was no palpable inguinal lymphadenopathy. His vital signs were otherwise stables and routine laboratory investigations including AFP, bHCG, LDH were within normal limits. The right testicle was normal with no masses palpated. A scrotal ultrasound showed a complex, predominantly solid appearing lesion measuring 1.3 × 1.2 cm in size between the left testicle and epididymis that was heterogeneous and. A CT chest abdomen and pelvis was done at the same time and showed no evidence of tumor recurrence, lymphadenopathy or other foci of disease.

On physical exam, he had no evidence of inguinal lymphadenopathy. While neuroblastoma relapse was considered unlikely (although possible), a secondary malignancy was thought likely given his previous history of chemo and radiotherapy. The patient underwent an open exploration of his spermatic cord and testis via an inguinal approach. A well circumscribed mass was identified adjacent to the testis and inseparable from the epididymis. Frozen section was consistent with possible yolk sac tumor. For that reason, he underwent a left open radical orchiectomy via an inguinal approach; a lymph node dissection was not performed. He did well postoperatively and was discharged home on postoperative day 1. Final pathology revealed papillary cystadenoma of the epididymis. On follow up in the clinic, he was doing well with no complaints. Follow up brain MRI and CT of chest/abdomen/pelvis to rule out VHL were without significant findings.

3. Pathology

Gross pathology revealed a cystic mass infiltrating into the epididymis with a normal testicle just above the mass (Fig. 1). Hematoxylin and eosin (H&E) stain shows the epididymal duct with the papillary neoplasm and papillary projections into the cysts that are lined by cuboidal clear cells consistent with the diagnosis of PCE (Fig. 2). The frozen section obtained in the OR (Fig. 3) shows proliferation of glandular like structures and a vague mucocystic appearance, which led to the intraoperative diagnosis of yolk sac tumor. On further inspection of the same image, the papillary projections are seen in the cysts. Immunostaining for CK7 was strongly positive (Fig. 4), and negative for CK20, CD10 and AFP (Fig. 5) consistent with final diagnosis of clear cell papillary cystadenoma of the epididymis.

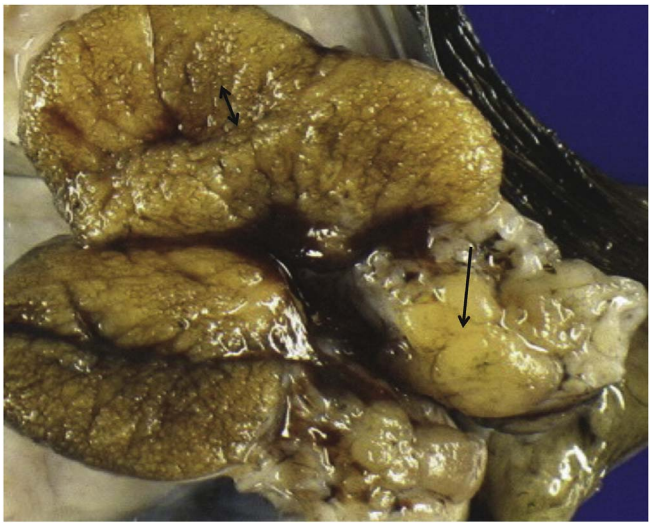

Fig. 1. Gross pathology of specimen showing the cys8c mass (arrow) and normal tes8cle just above (double headed arrow).

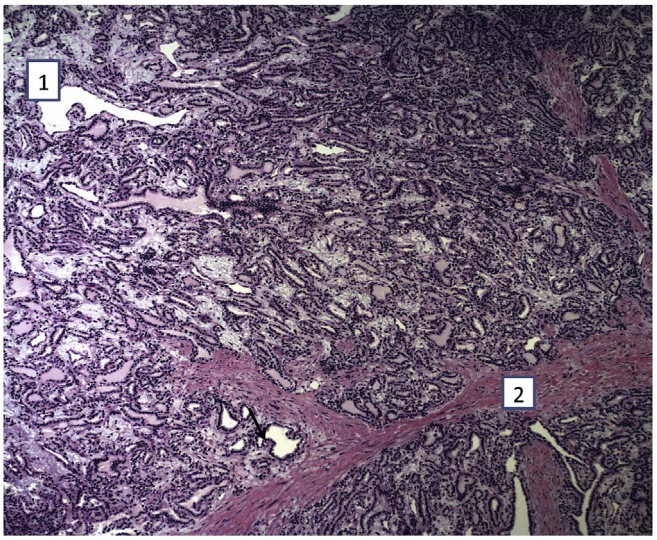

Fig. 2. H&E stain of Papillary cystadenoma of the epididymis. Epididymal duct with papillary neoplasm lined by cuboidal lear cells consistent with diagnosis. Papillary architecture is noted with cuboidal clear cells (1), stroma and (2) papillary protrusions into the cysts (arrow).

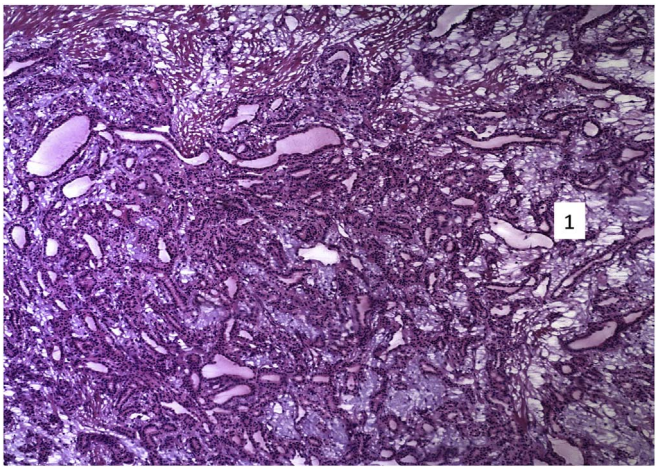

Fig. 3. Frozen section obtained in OR Proliferation of glandular like structures (1) and vague mucocystic appearance, led to intraoperative diagnosis of yolk sac tumor.

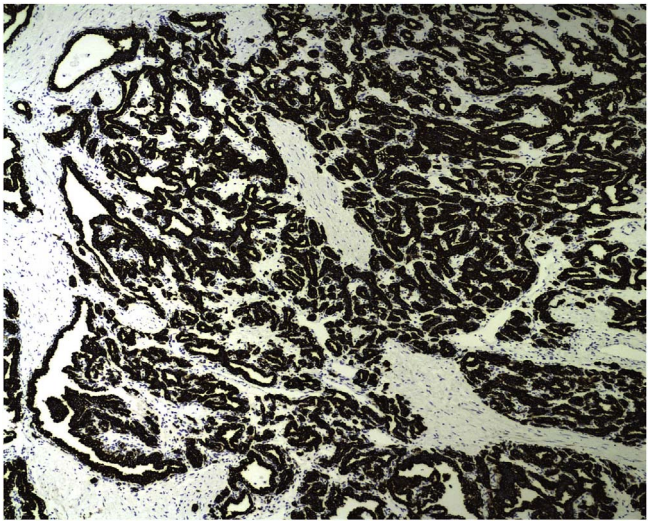

Fig. 4. CK7 stain positive, consistent with diagnosis of papillary cystadenoma of epididymis.

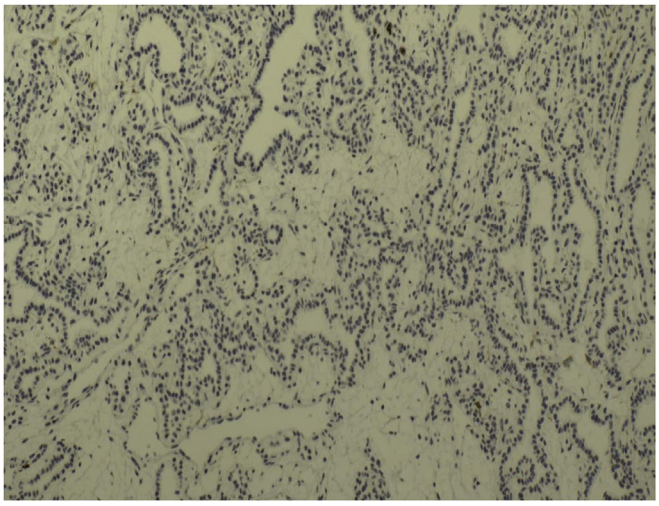

Fig. 5. AFP stain negative, consistent with diagnosis. AFP stain is typically positive in yolk sac tumors.

4. Discussion

This is the first report of a papillary cystadenoma of the epididymis in a prepubertal male. To date, the youngest reported patient with a diagnosis of papillary cystadenoma of the epididymis was 16. PCE bears close resemblance to renal cell carcinoma (RCC) on H&E staining [4]. In cases in which unilateral PCE is suspected, immunohistochemical stains for CD10 which is present in RCC but negative in PCE must be performed to rule out metastatic renal cell carcinoma. While VHL should be ruled out for patients who present with synchronous bilateral papillary cystadenoma of the epididymis, most experts discourage extensive testing in a patient presenting with unilateral disease [5].

The Childhood Cancer Survivor Study and International Neuroblastoma Risk Group have reported an 18 fold increased risk over matched controls for the development of secondary neoplasms in patients treated for high-risk neuroblastoma [6]. Leukemias are the most common of these neoplasms but soft tissue sarcomas, as well as carcinomas of the skin, thyroid, lungs and kidneys have been reported. However, there have been no previous reports of secondary paratesticular or testicular neoplasms. There have been several reports of paratesticular neuroblastoma as a site of metastatic disease from neuroblastoma. A retrospective review of 24 testicular and paratesticular tumors in children by Trobs et al. identified 13 germ cell tumors, 4 sex cord stromal tumors, 3 cases of paratesticular rhabdomyosarcoma and three cases of metastasis, one of which was from neuroblastoma [7].

The metachronous occurrence of PCE following the successful treatment of neuroblastoma may represent wholly unrelated neoplastic processes or PCE may have arisen as an uncommon sequelae of the multimodality chemotherapy and radiotherapy that is typically used to treat high risk neuroblastoma. Interestingly, allelic loss of the VHL gene on chromosome 3 has been discovered in benign papillary tumors presenting with VHL and deletions of the same region of the short arm of chromosome 3 (often in association with deletions of 11q) have been observed in a subset of aggressive neuroblastoma [8]. Given that PCE represents characteristic papillary histology, it is possible that this relates to an innate mutational event or a mutational event as a direct effect from chemoradiation.

5. Conclusion

This is a unique case, of a paratesticular mass with a rare histology-papillary cystadenoma of the epididymis, which has never been reported in a prepubertal male. Dissemination of this case is important as it emphasizes the importance of a broad differential in evaluating prepubertal males with paratesticular masses. In this particular case, given this patients' history of stage IV neuroblastoma, it was believed to represent a metachronous metastatic site. An intraoperative frozen section showed yolk sac tumor, which is a predominant histology of testicular masses seen in prepubertal males. This patient then underwent the standard of care for yolk sac tumor, a radical orchiectomy. This case emphasizes the importance of increasing awareness of rare and unique pathological entities that can be seen in an unexpected patient population.

Disclosure of conflicts of interest

There are no conflicts of interest and no disclosures from any of the authors listed.

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